REMARKS

Claims 104-109, 113-118, 131-133, 137, 144, 148 and 149 have been canceled. Claims 126, 128, 130, 134, 135, 136, 141 and 142 have been amended. Claims 150-184 have been added. After entry of the above-mentioned amendments, claims 126-130, 134-136, 141-143 and 150-184 will be pending in the application.

The specification has been amended to indicate that the invention was made with government support and that the government has certain rights in the invention, as required by 35 U.S.C. § 202(c)(6) and 37 C.F.R. §§ 401.3(a) and 401.14(f)(4). Typographical errors have also been corrected.

Claims 126, 128, 130, 134, 135, 136, 141 and 142 have been amended to change the dependencies on canceled independent claims 146 or 147 to dependencies on new independent claims 150 and 151.

Claims 126, 128, 130, 134, and 135 have been amended to delete the word "target", which is not present in new claim 150.

Claim 128 has been amended to delete the term "naturally" so that the resulting claim is directed to a method of detecting nucleic acids associated with an etiological agent. Support for this amendment is found, e.g., on p. 31, lines 17-22 of the specification.

Claim 135 has been amended to include the term "associated with" so that the resulting claim is directed to a method of detecting nucleic acids associated with (i.e., present) or absent in thalassemic subjects. Support for this amendment is found, e.g., on p. 32, lines 14 to 21 of the specification.

Claim 141 has been amended so that the resulting claim is directed to a method of detecting the presence or absence of hormonal receptor sites on the surface of malignant cells.

Support for this amendment can be found, e.g., on p. 40, lines 18-20 of the specification.

Claim 142 has been amended to change the term "diagnostic for a tumor cell" to "associated with a tumor cell". Detection of expression of certain polypeptides, such as α-fetal protein or carcinoembryonic antigen, were well known as useful in the diagnosis and/or prognosis of the fate of tumor cells at the time of filing of the priority application (April 17, 1981).

New claims 150 and 151 are amended versions of claims 146 and 147 which were added in the amendment dated July 24, 1992, and renumbered by the Examiner as claims 148 and 149 (see p. 3 of the Office Action dated September 29, 1992 (paper number 23)). New claims 150 and 151 clarify that the deazapurine referred to is a 7-deazapurine. Support for this amendment can be found, e.g., on p. 7, line 10 to p. 8, line 14; p. 25, line 3 to p. 26, line 7; p. 4, lines 1-33; and p. 10, line 21 to p. 11, line 17. Claim 150 no longer contains the reference to the signaling moiety being capable of producing a detectable signal when the compound is incorporated into a double-stranded ribonucleic acid or deoxyribonucleic acid. Note that the criteria for "A" set forth on pages 9-10 of the specification, as noted by the Examiner in the Office Action dated 10/21/91 (see pages 4-7)(paper 15) and as expanded upon by Applicants in the previous Amendment dated April 21, 1992 (see pages 15-22), do not include the requirement that the signaling moiety being capable of producing a detectable signal when the compound is incorporated into a double-stranded ribonucleic acid or deoxyribonucleic acid. Thus, the signalling moiety may be detectable when it is incorporated into a double-stranded ribonucleic acid or deoxyribonucleic acid as well as after the compound has been incorporated into a double-stranded ribonucleic acid or deoxyribonucleic acid but is no longer in

that state. Other changes from claims 148 and 149 have been made in new claims 150 and 151, including the deletion of some steps from claim 151 concerning disrupting the cells and recovering cell surface fragments.

New claim 152 is directed to an embodiment of claim 150 wherein the "A" moiety is a ligand. Support for this claim is found, e.g., at p. 12, lines 6-35 of the specification.

Support for new claim 153, wherein the ligand is a hapten, antigen, cofactor, biotin or iminobiotin; new claim 154, wherein the ligand is dinitrophenol or lipoic acid or an olefinic compound; and new claim 155, wherein the ligand is allylamine, is found throughout the specification. See, e.g., p. 12, lines 7-35 of the specification. More specifically, support for the hapten DNP is found on p. 16, lns. 1-15; support for a cofactor ligand is found, on p.4, ln. 4 and p. 12, lns. 25-30, right column, in the listing of lipoic acid as a ligand (lipoic acid is a cofactor of a number of enzymes); support for "A" being an "olefinic compound" (e.g., allylamine) is found on p. 20, lines 10-20 of the specification.

Support for new claim 156, wherein the polypeptide is capable of forming a complex via binding with moiety A can be found, e.g., on p. 12, lines 1-5 of the specification.

Support for new claim 157, wherein the detectable polypeptide is an antibody, an enzyme, streptavidin or avidin, if found throughout the specification. Furthermore, these compounds are known ligands for a hapten, an antigen, a cofactor, biotin or iminobiotin.

Support for new claim 158, wherein the antibody is a monoclonal antibody, a well known type of monospecific antibody, is found, e.g., on p. 36, lines 1 and 12 of the specification.

Support for new claim 159, wherein the sample is contacted with the detectable polypeptide after hybridization of

the compound or compounds to the nucleic acid, can be found, e.g., on p. 32, lines 6-10, and p. 49, lines 5-9 of the specification.

Support for new claim 160, wherein an indicator molecule is associated with or bound to the detectable polypeptide, can be found throughout the specification. See also, e.g., canceled claim 109.

Support for new claim 161, wherein the indicator molecule is fluorescent, electron dense, or is an enzyme, is found, e.g., on p. 2, lines 8 to 10 of the specification.

Support for new claim 162, wherein the enzyme is either alkaline phosphatase, peroxidase, or β-galactosidase, can be found, e.g., on p. 2, lines 11-12 and p. 28, lines 5-6.

Support for new claim 163, wherein the fluorescent group is either fluorescein or rhodamine, is found, e.g. on p. 2, line 9 and page 28, lines 3-4.

Support for new claim 164, wherein the electron dense indicator molecule is either ferritin, hemocyanin, or colloidal gold, is found, e.g., on p. 2, lines 10-11 and page 28, lines 4-5.

Support for new claims 165-167, which are related to direct and indirect detection methods, can be found throughout the specification. Support for linking the polypeptide to an indicator molecule is found, e.g., at p. 2, lines 7-14, p. 35, line 28 to p. 38, line 16, and p. 38, line 18 to p. 39, line 9 of the specification. Support for sandwich and multi-layered sandwich methods of immunological detection are set forth in great detail in the specification and exemplified at pp. 34-37.

Support for new claims 168-169, involving the use of at least two differently labeled compounds to detect nucleic acids, is found in Example 9, parts I and II in the

specification. See, e.g., p. 49, lines 5 -15 and p. 50, lines 7-12 of the specification.

Support for new claim 170, wherein the "A" moiety comprises an indicator molecule, is found at p. 9, lines 6-10; p. 9, line 32 to p. 10, line 2; and p. 22, lines 15-17 of the specification. Specifically, these disclosures teach that the probe (i.e., the "A" moiety") may react specifically with chemical reagents to provide a detection system. It would be readily apparent to one skilled in the art that in order for "A" to react directly with chemical reagents and thereby provide a detection system, "A" itself would be capable of detection. At pp. 22, an embodiment is disclosed wherein biotin- or iminobiotin-containing nucleotides may be radiolabeled.

Support for new claim 171, wherein an indicator molecule is fluorescent, electron dense, or is an enzyme, is found, e.g., on p. 2, lines 8 to 10 of the specification.

Support for new claim 172, wherein the enzyme is either alkaline phosphatase, peroxidase, or β-galactosidase, can be found, e.g., on p. 2, lines 11-12, p. 28, lines 5-6 and p. 38, lines 19-20 of the specification.

Support for new claim 173, wherein the fluorescent group is either fluorescein or rhodamine, is found, e.g. on p. 2, line 9 and page 28, lines 3-4.

Support for new claim 174, wherein the electron dense indicator molecule is either ferritin, hemocyanin, or colloidal gold, is found, e.g., on p. 2, lines 10-11 and page 28, lines 4-5.

Support for new claim 175, wherein the signalling moiety is capable of producing a detectable signal when the compound is incorporated into a double-stranded ribonucleic acid, deoxyribonucleic acid duplex, or DNA-RNA hybrid, is found, e.g., on p. 10, line 34 to p. 11, line 2 of the specification.

Support for new claim 176, wherein the detecting step is carried out during hybridization, can be found, e.g., on p. 32, lines 6-10, and p. 49, lines 5-9 of the specification.

Support for new claim 177, wherein the nucleic acid is immobilized on a solid support, can be found, e.g., on p. 50, lines 29-31 and lines 12-15 of the specification.

Support for new claim 178, wherein the moiety A comprises at least 5 carbon atoms, can be found, e.g., on p. 13, line 5 of the specification.

Support for new claim 179, wherein the moiety A is non-aromatic, can be found, e.g., on p. 13, lines 2-3 of the specification.

Support for new claim 180, wherein B is selected from the group consisting of uracil, cytosine, deazaadenine, deazaguanine, can be found, e.g., on p. 11, lines 35-36 of the specification.

Support for new claim 181, wherein the linkage group comprises an olefinic bond at the α-position relative to B, can be found, e.g., on p. 13, lines 13-15 of the specification.

Support for new claims 182 and 183, wherein the linkage group comprises the moiety $-CH=CH-CH_2-NH-$ or $-CH=CH-CH_2-O-CH_2-\underset{\displaystyle OH}{\underset{|}{CH}}-CH_2-NH-$, respectively, can be found, e.g., on p. 13, lines 28-31 of the specification.

New claim 184 replaces canceled claims 131 to 133. The reference to the microorganism Neisseria meningitidis in canceled Claim 131 is dropped and the various antibiotics referred to in canceled claims 131-133 are listed in a Markush group instead of being claimed separately. Support for new claim 184 is found, e.g., on p. 31, lines 24-31 and p. 51, lines 1-7 of the specification.

Applicants respectfully submit that the above amendments do not constitute new matter.

1. Informalities

Applicants have amended the title recite "Methods of Using Labeled Nucleotides". Applicants believe this title more precisely indicates what the claimed invention is directed to, as requested by the Examiner. Applicants have also corrected the spelling errors on pages 38 and 47 of the specification which were pointed out by the Examiner. Applicants submit that the Examiner's objections have been overcome and respectfully request that the related objections be withdrawn.

The Examiner states that none of the references cited in parent application serial number 06/496,915 or cited on PTO Form-1449 filed August 7, 1989 in the instant application have been considered in the instant application because of a lack of access to said parent application as well as a lack of copies of the cited references filed in the instant application. Applicants will forward shortly a new IDS, PTO Form-1449, references cited therein and appropriate fee, for consideration by the Examiner. Most, if not all, of the references specifically referred to herein will be included in that IDS for the Examiner's convenience.

2. Rejection Under 35 U.S.C. § 112, first paragraph

The specification is rejected under 35 U.S.C. §112, first paragraph for failing to provide an enabling disclosure. Claims 131-133, 135, 141, 143 and 144 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

A. It is the Examiner's position that the none of the genes or nucleic acids specifically listed on pages 4 to 5 of the Office Action are enabled in the instant disclosure

Applicants respectfully disagree with the Examiner's position that none of the listed genes or nucleic acids are enabled in the instant disclosure.

First, Applicants wish to point out that claims 131-133 and 144 have been canceled without prejudice, thereby rendering the rejection of these claims moot. New claim 184, which replaces canceled claims 131 to 133, does not contain reference to the microorganism Neisseria meningitidis and refers to the various antibiotics in a Markush group.

At the time of filing of the priority application (April 17, 1981), many of the DNA molecules associated with antibiotic resistance in the microorganisms referred to in new claim 184 were widely known in the field to which the invention pertains and it would have been a routine matter to one of skill in the art to obtain the DNA sequences associated with the claimed antibiotic resistance. Furthermore, as taught in the specification on p. 51, lines 1-7, any antibiotic resistance for which a particular gene has been identified could be characterized using, as a probe, the DNA sequence which is contained in the antibiotic resistance gene. Therefore, Applicants respectfully submit that the listed genes or nucleic acids are enabled in the specification.

For specific references to specific DNA molecules associated with antibiotic resistance in microorganisms, see, e.g., the following references:

* concerning tetracycline resistance in Staphylococcus aureus: Groves, D.J., "Interspecific Relationships of Antibiotic Resistance in Staphylococcus-Sp - Isolation and Comparison of

Plasmids Determining Tetracycline Resistance in Staphylococcus-Aureus and Staphylococcus-Epidermis, Can. J. Microbiol. 25(12):1468-1475 (1979); Kono, M. et al., "Isolation of the Specific Protein from the Tetracycline Resistance Plasmid in Staphylococcus-Aureus", Current Chemotherapy, pp. 448-449 (1978); Schaefler, S. et al., "Complex Locus for Chromosomal Tetracycline Resistance in Staphylococcus-Aureus", Current Chemotherapy, pp. 446-447 (1978); Shafferman, A. et al., "Cleavage Maps of a Tetracycline Plasmid from Staphylococcus-Aureus", J. Bacteriol. 134(1):345-348 (1978); Inoue, M. et al., "A Bacterio-Phage S-1 Derivative that Transduces Tetracycline Resistance to Staphylococcus-Aureus", Virology 68(2):544-546 (1975); Asheshov, E.H., "The Genetics of Tetracycline Resistance in Staphylococcus-Aureus", J. Gen. Microbiol. 88(1):132-140 (1975) and Sompolinsky, D. et al., "Plasmid-Borne Resistance to Tetracycline", Contributions to Microbiology and Immunology, Vol. 6, Extrachromosomal Inheritance in Bacteria; 23rd Annual Oholo Biological Conference, Safed, Israel, Apr. 21-24, 1978,. XIV+238P. S. Kaarger: Basel Switzerland; New York, N.Y. USA (Hertman I. et al. (Ed.)) 0(0):pp. 198-209 (1979);

* concerning tetracycline resistance in Pseudomonas aeruginosa: Hedstrom, R.C. et al., "Tetracycline Resistance in Pseudomonas-Aeruginosa Containing the R Plasmid Rp-1", Annual Meet. Am. Soc. Microbiol. 80(0):Abstract 1808 (1980) and Sompolinsky, D. et al., "Plasmid-Borne Resistance to Tetracycline", Contributions to Microbiology and Immunology, Vol. 6, Extracrhromosomal Inheritance in Bacteria; 23rd Annual

Oholo Biological Conference, Safed, Israel, Apr. 21-24, 1978, XIV+238P, S. Kaarger: Basel Switzerland; New York, N.Y. USA (Hertman I. et al. (Ed.)) 0(0):pp. 198-209 (1979);

* concerning tetracycline resistance in Streptococcus pyrogenes: Ubakata, K. et al., "Transduction of drug resistance to tetracycline, chloramphenicol, macrolides, lincomycin, and clindamycin with phages induced from Streptococcus pyrogenes", J. Antibiot. 28:681-688 (1975);

* concerning tetracycline and penicillin resistance genes in Neisseria gonorrhoeae: Biswas, G. et al., "Chromosomal Location of Antibiotic Resistance Genes in Neisseria-Gonorrhoeae", J. Bacteriol. 125(3):1207-1210 (1976) and Warner, P.F. et al., "Polygenes and Modifier Genes for Tetracycline and Penicillin Resistance in Neisseria gonorrhoeae", J. Gen. Microbiol. 117:103-110 (1980).

Further, with respect to claim 135, at the time of filing of the priority application (April 17, 1981), it was also widely known in the field to which the invention pertains that the presence and/or absence of specific nucleic acid sequences were associated with thalassemia and that this information could be used to diagnose thalassemia. Specifically with respect to nucleic acid sequences which are absent, see, e.g., Van Der Ploeg, L.H.T. et al., "Gamma-Beta Thalassemia Studies Showing That Deletion of the Gamma and Delta Genes Influences Beta Globin Gene Expression in Man", Nature (Lond) 283:637-647 (1980); Lauer, J. et al., "The Chromosomal Arrangement of Human Alpha-Like Globin Genes - Sequence Homology and Alpha Globin Gene Deletions", Cell 20(1):119-130 (1980); and Fritsch et al., "Characterization of Deletions Which Affect the Expression of

Fetal Globin Genes in Man", Nature (Lond) 279:598-603 (1979). Knowledge of the polynucleotide which is absent in thalassemic subjects but present in normal subjects would enable one of skill in the art to use a "polynucleotide complementary to the sequence which is absent in thalassemic subjects" and to determine from a failure to detect its presence in a sample from that subject that that subject had thalassemia due to the absence of the particular polynucleotide which is absent in thalassemic patients.

Finally, with respect to claim 143, at the time of filing of the priority application (April 17, 1981), it was widely known in the field to which the invention pertains that specific genes or nucleic acid sequences encoded the polypeptide α-fetal protein. At least part of the nucleic acid sequence of α-fetal protein was known and used as a specific probe for complementary nucleic acid sequences at that time. See, e.g. Innis, M.A. et al., "Alpha Feto Protein Gene Expression -- Partial DNA Sequence and Carboxyl Terminal Homology to Albumin", J. Biol. Chem. 255:8994-8996 (1980) and Law, S. et al., "Molecular Cloning of DNA Complementary to a Mouse Alpha Feto Protein Messenger RNA Sequence", Gene 10(1):53-62 (1980).

B. The Examiner notes that claim 141 cites detecting abnormal hormonal receptor sites. It is the Examiner's position that the specification lacks any enablement or guidance as to what structures, from those given in claim 140, or detection methods are needed to detect "abnormal" receptor sites.

Applicants have amended claim 141 to delete the reference to "abnormal" hormonal sites, thereby obviating the Examiner's rejection of that claim for lack of enablement of structures or methods needed to detect "abnormal" hormonal receptor sites. Claim 141 has also been amended to depend on

new claim 151, since the structures given in new claim 151 are used to detect the hormonal receptor sites referred to in amended claim 141. Applicants, therefore, respectfully request that this rejection be withdrawn.

In view of the above amendments and remarks, Applicants submit that the application is fully enabled in its present form and that no additional material is necessary to either support the claims or provide an adequate disclosure of the invention. Thus, Applicants respectfully request that the rejection of claims 131-133, 135, 141, 143 and 144 under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

3. Rejection Under 35 U.S. C. § 112, First Paragraph

Claims 104-109, 113-118, 126-137, 141-144, 148, and 149 are rejected under 35 U.S.C. § 112, first paragraph, on the ground that the disclosure is enabling only for claims limited to modification of 7-deazapurines (claim moiety B) at the 7-position or modification of pyrimidines (claim moiety B) at the 5-position, for attachment of moiety A. This rejection is directed to the non-enablement of the C-8 purine modification. First, Applicants note that claims 104-109, 113-118, 137, 148 and 149 have been canceled, thereby rendering the rejection of those claims moot. With respect to the remaining claims, Applicants reiterate that the specification states that methods for attaching moieties to pyrimidine and purine rings were known at the time of filing of the priority application and that it is well established that a specification need not disclose what is well known in the art. It is sufficient that the specification sufficiently disclose the invention to enable those skilled in the art to make and use it. In re Buchner, 929 F.2d 660, 661 (Fed. Cir. 1991), citing Lindemann Maschinenfabrik GMBH v.

American Hoist & Derrick Co., 730 F.2d 1452, 1463 (Fed. Cir. 1984). What is conventional knowledge will be read into the disclosure. In re Howarth, 654 F.2d 103, 105 (C.C.P.A. 1981).

In the instant case, the specification need not detail the specifics of these reactions since it was well known in the art how to generate reactive moieties at the 8-position of a purine before April 17, 1981, the time of filing of the earliest application from which this application claims priority.

More specifically, in the instant specification, Applicants teach the addition of linkers and/or labels to a nucleic acid. Applicants exemplify preparing reactive moieties by the palladium-catalyzed olefination of organo-mercurial compounds at the 5-position of a pyrimidine. Other reactions capable of attaching a reactive moiety to the 8-position of a purine to which a linker arm and/or label could be attached were also well known in the art at the time of filing of the application, as discussed further below.[1] For example, Lee et al., "8-(6-Aminohexyl)-Amino-Adenine Nucleotide Derivatives for Affinity Chromatography", Arch. Bioch. Biophys. 163:561-569 (1974) discloses a method of attaching a (6-aminohexyl)amino group (a linker with a reactive terminal group) to the 8-position of adenosine monophosphate (a purine). See especially p. 562, col. 2. Further with respect to the enablement of modification of the C-8 position of a purine, see column 16 of U.S. Patent No. 4,230,797, filed April 10, 1978 and pages 13-14 of the related British specification 1,548,741 (both of record). See also, Trayer et al., "Preparation of Adenosine Nucleotide Derivatives Suitable for Affinity Chromatography", Biochem. J. (1974) 139:609-623 (which is reference 24 on the bottom of column 26 in U.S. Patent No. 4,230,797). On page 610, column 1,

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1 But none of the following references disclose Applicants' invention involving incorporation of modified nucleotides into a polynucleotide.

Trayer et al. states that "[t]he synthetic methods employed [in the described study describing the synthesis of a series of chemically-defined AMP, ADP and ATP derivatives that contain primary amino groups suitable for coupling to CNBr-activated agarose] are all in fairly common use." This column further states that "[p]rocedures are given for attachment of the adenosine phosphate through the . . . 8-position of the adenine nucleus". Thus, Applicants reiterate their position that other reactions capable of attaching a reactive moiety to the 8-position of a purine to which a linker arm and/or label could be attached were well known in the art at the time of filing of the application and, thus, the C-8 purine modification referred to in the specification is enabled.

Furthermore, the following references (all of record in the parent application) demonstrate that cyclic phosphates can be functionalized at the 8-position and that this was known to one of skill in the art. For example, Shuman et al., U.S. Patent No. 3,915,958, "6-substituted purine nucleotides" discloses a process for preparing 8-bromoadenosine 3',5'-cyclic phosphate-N^1-oxide. See example 1. Christensen et al., U.S. Patent No. 3,968,101, "8-substituted cyclic nucleotides by free radical alkylation and acylation" discloses a method for introducing alkyl and acyl groups directly onto the 8-position of existing guanosine 3',5'-cyclic phosphate molecules (see columns 3-4) and also disclose a $-NH_2$ reactive group at the end of the substituent (see structures 15 and 16 in column 6). Christensen et al. also cite articles disclosing the synthesis of a number of 8-alkylthio-, 8-arylthio- and 8-alkylamino-cGMP derivatives, along with 8-hydroxy- and 8-bromo-cGMP (see column 2, lines 60-70). Finally, Yokota et al., U.S. Patent No. 4,048,307, "Cyclic adenosine monophosphate 8-substituted derivatives" (issued Sept. 13, 1977) discloses cyclic adenosine

monophosphate derivatives containing alkyl substituents added to the 8-position of 3',5' cyclic-monophosphate. Yokota et al. also states that other 8-substituted c-AMP derivatives, such as alkylamino or alkylthio derivatives, were known in the art. See col. 2, lns. 22-33. Given the teachings of the specification that a detectable moiety can be attached to a nucleotide base having a reactive terminal group and the teachings of the art, as evidenced, for example, by the above-cited references, one of ordinary skill in the art would have found it a routine exercise to attach a linker arm and/or label to the 8-position of a purine. Applicants therefore submit that one skilled in the art would have known how to attach linkers and/or labels to the 8-position of a purine given the disclosure of the application and what was widely known in the art. Furthermore, Applicant need not have made reference to these widely known methods.

In view of the above amendments and remarks, Applicants submit that all of the pending claims are enabled and respectfully request that the rejection of claims 104-109, 113-118, 126-137, 141-144, 148, and 149 under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

4. Rejection Under 35 U.S.C. §112, Second Paragraph

Claims 113-118 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention on the ground that claim 113 is vague and indefinite in that the polypeptide complexing practice therein claimed is unclear or whether the polypeptide can bind anywhere on the compound of claim 125 [sic] without specifically binding to moiety A.

Claims 113-118 have been canceled, thereby rendering the rejection of these claims moot.

In view of the foregoing amendments and remarks, Applicants respectfully request that the rejection of claims 113-118 under 35 U.S.C. § 112, second paragraph, be reconsidered and withdrawn.

5. Rejection Under 35 U.S.C. §112, Fourth Paragraph

Claims 108 and 117 are rejected under 35 U.S.C. § 112, fourth paragraph, as being of improper dependent form for failing to further limit the subject matter of a previous claim.

Claims 108 and 117 have been canceled, thereby rendering the rejection of these claims moot.

In view of the foregoing amendments and remarks, Applicants respectfully request that the rejection of claims 108 and 117 under 35 U.S.C. §112, fourth paragraph be reconsidered and withdrawn.

6. Rejection Under 35 U.S.C. §101

Claims 141-144 are rejected under 35 U.S.C. § 101 on the ground that there is no evidence given in the instant disclosure that supports the diagnostic utility claimed as detecting malignant cells (claim 141) or diagnosing a tumor cell (claims 142-144). The Examiner states that such diagnostic utility must be supported by evidence that supports definite and currently available utility.

Claim 144 has been canceled, thereby rendering the rejection of this claim moot.

Claim 141 has been amended so that the resulting claim is directed to a method of detecting the presence or absence of hormonal receptor sites on the surface of malignant cells. The presence of cyclic AMP binding proteins in malignant cells was well known before April 17, 1981, the time of filing of the earliest application from which this application claims

priority. Applicants believe that the amendment to claim 141 overcomes this ground for rejection.

Claim 142 has been amended to change the term "diagnostic for a tumor cell" to "associated with a tumor cell". Detection of expression of certain polypeptides, such as α-fetal protein (claim 143) or carcinoembryonic antigen (canceled claim 144) were well known as useful in the diagnosis and/or prognosis of the fate of tumor cells before April 17, 1981, the time of filing of the earliest application from which this application claims priority. Applicants believe that the amendment to claim 142 overcomes this ground of rejection.

In view of the foregoing amendments and remarks, Applicants respectfully request that the rejection of claims 141-144 under 35 U.S.C. §101 be reconsidered and withdrawn.

CONCLUSION

In view of the foregoing amendments and remarks, Applicants submit that the instant application is in condition for allowance. Favorable reconsideration and an action passing this case to issue are therefore respectfully requested.

Respectfully submitted,

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